Journal of the Neurological Sciences 328 (2013) 24–27

Contents lists available at SciVerse ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

# Auditory evoked potentials and vestibular evoked myogenic potentials in evaluation of brainstem lesions in multiple sclerosis

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ARTICLE INFO

*Article history:*
Received 24 December 2012
Received in revised form 5 February 2013
Accepted 7 February 2013
Available online 13 March 2013

*Keywords:*
Auditory evoked potentials
Vestibular evoked myogenic potentials
Brainstem
Multiple sclerosis

ABSTRACT

*Objective:* The aim of this study was to determine the roles of magnetic resonance imaging (MRI), auditory evoked potentials (AEP) and vestibular evoked myogenic potentials (VEMP) in the evaluation of brainstem involvement in multiple sclerosis (MS).
*Patients and methods:* Altogether 32 patients with the diagnosis of MS participated in the study. The following data was collected from all patients: age, gender, Expanded Disability Status Scale (EDSS) score, brainstem functional system score (BSFS) (part of the EDSS evaluating brainstem symptomatology), and involvement of the brainstem on the brain MRI. AEP and ocular VEMP (oVEMP) and cervical VEMP (cVEMP) were studied in all patients.
*Results:* BSFS, MRI, AEP, oVEMP and cVEMP involvement of the brainstem was evident in 9 (28.1%), 14 (43.8%), 7 (21.9%), 12 (37.5%) and 10 (31.0%) patients, respectively. None of the tests used showed statistically significant advantage in the detection of brainstem lesions. When combining oVEMP and cVEMP 18 (56.3%) patients showed brainstem involvement. This combination showed brainstem involvement in greater percentage than BSFS or AEP, with statistical significance ($p = 0.035$ and $p = 0.007$, respectively).
*Conclusion:* VEMP is a reliable method in detection of brainstem involvement in MS. It is comparable with MRI, but superior to clinical examination or AEP.



## 1. Introduction

Multiple sclerosis (MS) is a chronic idiopathic demyelinating illness of the central nervous system and it is the leading cause of disability in young adults.

It is estimated that around 65% of MS patients had one or more brainstem or cerebellar manifestations in the course of the disease [1]. The presence of infratentorial lesions has been associated with worse Expanded Disability Status Scale (EDSS) score at follow-up and is one of the major predictive factors for future disability [2,3]. As well, several studies have shown that infratentorial lesions are related to long-term prognosis for patients with clinically isolated syndrome and thus may help to identify patients at high risk for earlier occurrence of clinically relevant disability [4,5].

Although there is relatively good correlation between brainstem impairment and T2 lesion burden, the association between clinical findings and radiological extent of involvement generally is poor (the so called clinico-radiological paradox) [6,7].

Evoked potentials are reliable procedures to predict disability in MS patients. Index of global EP alteration (EP score) which combines alterations in visual evoked potentials, AEP, motor and somatosensory evoked potentials showed significant correlation with EDSS score at the time of neurophysiological study and at 1, 3 and 5 years of follow-up [8]. On the other hand, AEP alone are insufficient in detecting subclinical lesions of the brainstem [9]. However, newer brainstem evoked potentials like ocular and cervical vestibular evoked myogenic potentials (oVEMP and cVEMP) have shown promise in detecting brainstem involvement in MS [10].

The aim of the present study was to determine the role of MRI, AEP and VEMP in the evaluation of brainstem involvement in MS.

## 2. Patient and methods

### 2.1. Patients

Patients with the diagnosis of relapsing–remitting MS according to the revised McDonald's criteria were prospectively included in the study [11]. The following data was collected from all patients: age,

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http://dx.doi.org/10.1016/j.jns.2013.02.005

gender, Expanded Disability Status Scale (EDSS) score, brainstem functional system score (BSFS) (part of the EDSS evaluating brainstem symptomatology), and involvement of the brainstem on the brain MRI. All participants were informed about the details of the experiment and they all signed informed consent forms. Study was approved by the Ethical Committee of the University Hospital Centre Zagreb.

### 2.2. Auditory evoked potentials

During the experiment participants sat or lay in a relaxed position in a slightly darkened room. Their eyes were closed in order to avoid ocular artifacts. Activity was recorded with four surface disk electrodes. Active electrodes were situated on the mastoids on both sides and referred to the vertex electrode Cz. Frontal electrode Fz was used as ground electrode.

A pair of headphones delivered the stimuli. The stimulation rate was 10 Hz and stimuli were acoustic clicks of 0.1 ms duration. At the beginning of the experiment the perceptive threshold for each participant for each ear was assessed. During the experiment, the intensity of stimulation delivered to the tested ear was 70 dB higher than the perceptive threshold. In the same time the white noise with the intensity 30 dB lower than the intensity delivered to the tested ear was delivered to the contralateral ear in order to reduce the effect of bone conductivity. Each series consisted of 1000 stimuli and was repeated twice for each ear in order to provide reproducibility. Recordings were performed using Medelec Synergy, Oxford Instruments, UK. Automated analysis according to the normative values was performed with the same system.

The results of AEP were regarded either as pathological or normal according to the normative values for the laboratory.

### 2.3. Vestibular evoked myogenic potentials

During the experiment participants sat in comfortable chair. Patients were instructed to slightly move their head away from the back of the chair and push it forward in order to activate the sternocleidomastoid muscle. The contraction of the muscle was maintained due to the cooperation of patients in maintaining the same position during the test. Participants were also instructed to direct their gaze to the ceiling in order to activate ocular muscles. The evoked response from the SCM was recorded from the active surface electrode placed on the belly of the SCM of the stimulated side and referred to the surface electrode placed on the tendon of the same SCM. The evoked response from the OM was recorded from two surface electrodes situated 2 cm below the contralateral eye. Active electrode was situated closer to the eye and referred to the reference 1 cm below. The stimuli were delivered by a pair of headphones in a series of 50 trails to one ear at a time and repeated two times for each ear in order to provide reproducibility. The presented stimuli were acoustic clicks of 1 ms duration at the intensity of 130 dB SPL and the stimulation frequency of 1 Hz. Recording were performed using a Brain Products Brain Vision Recorder and the analysis of the recorded data was performed using a Brain Products Brain Vision Analyzer. Signals were filtered with bandpass filter from 5 Hz to 1000 Hz. For the purpose of the analysis signals were divided in segments of 120 ms duration (20 ms before the stimulus and 100 ms after the stimulus) and averaged for each set of 50 trials. From the averaged responses from the two sets, the grand average was computed and used for further analysis. We used baseline normalized values of the SCM amplitude data instead of the absolute value of amplitude, because absolute amplitude of the evoked response depends on the amplitude of the muscle activity (muscle contraction) and is not a reliable measure. The baseline normalized value of amplitude is calculated by dividing the absolute peak to peak amplitude (P13-N23) with mean value of rectified activity of muscle in the period prior the stimulus.

The results of oVEMP and cVEMP were regarded either as pathological or normal according to the normative values for the laboratory.

### 2.4. Statistical analysis

Statistic analysis was performed using IBM SPSS 19.0 (Chicago, IL). We used the McNemar's test, which evaluates changes in related or paired binomial attributes, whether changes in one direction is significantly greater than that in the opposite direction. Phi correlation was performed for MRI, AEP, VEMP and clinical brainstem involvement. p values less than 0.05 were considered significant.

## 3. Results

Altogether 32 patients participated in the study, 19 females and 13 males, aged from 21 to 49 years (median 29 years). Median EDSS was 2 (ranging from 0 to 3.5).

Clinical involvement of the brainstem was evident in 9 (28.1%) patients, meaning that BSFS was greater than or equal to 1. Brainstem lesions were evident on MRI in 14 (43.8%) patients.

In only 7 (21.9%) patients AEP showed brainstem involvement. In contrast oVEMP showed brainstem involvement in 12 (37.5%) and cVEMP in 10 (31.0%) patients. When combining oVEMP and cVEMP 18 (56.3%) patients had signs of brainstem involvement.

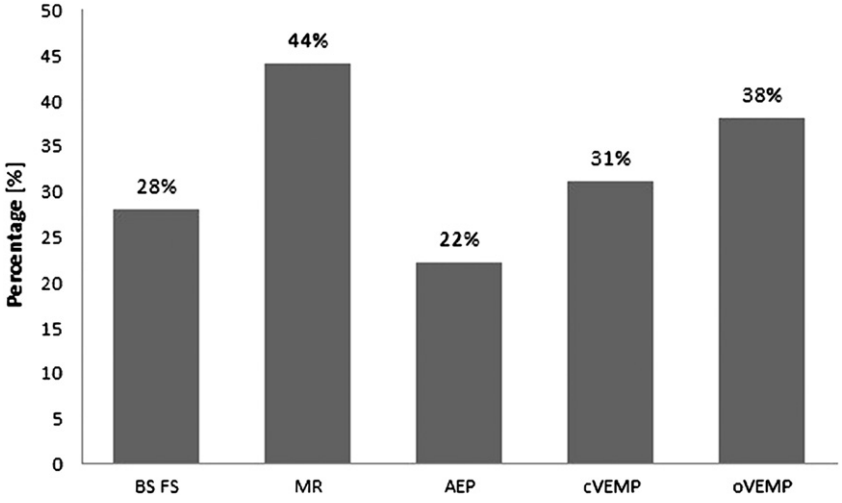


**Fig. 1.** Clinical, MRI and evoked potential findings showing brainstem involvement in the studied cohort.